FILE 'USPAT' ENTERED AT 14:22:41 ON 23 JUL 1998

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=> e adermann/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	15	ADERMAN, WAYNE L/IN
E2	USPAT	3	ADERMAN, WAYNE LOWELL/IN
E3	USPAT	0 -->	ADERMANN/IN
E4	USPAT	1	ADERMANN, DAVID A/IN
E5	USPAT	2	ADERMANN, KNUT/IN
E6	USPAT	1	ADERMANN, PETER/IN
E7	USPAT	2	ADERNECK, STEPHEN E/IN
E8	USPAT	1	ADERS, THOMAS D/IN
E9	USPAT	2	ADERS, WOLF KARLO/IN
E10	USPAT	1	ADERSKI, PENTCHO K/IN
E11	USPAT	1	ADERTON, GILBERT S/IN
E12	USPAT	5	ADES, ADRIAN R/IN

=> s e5; d 1-2 leg ab

L1 2 "ADERMANN, KNUT"/IN

US PAT NO: 5,767,239 [IMAGE AVAILABLE] L1: 1 of 2
DATE ISSUED: Jun. 16, 1998
TITLE: Process for preparing cardiodilatin fragments; highly purified cardiodilatin fragments and intermediate products for the preparation of same
INVENTOR: Hansueli Immer, Balsthal, Switzerland
Wolf-Georg Forssmann, Hanover, Federal Republic of Germany
Knut Adermann, Hanover, Federal Republic of Germany
Christian Klessen, Lauterecken,, Federal Republic of Germany
ASSIGNEE: Boehringer Mannheim GmbH, Mannheim, Federal Republic of Germany (foreign corp.)
APPL-NO: 08/737,927
DATE FILED: Dec. 2, 1996
ART-UNIT: 186
PRIM-EXMR: David Saunders
ASST-EXMR: F. Pierre VanderVegt
LEGAL-REP: Nikaido Marmelstein Murray & Oram LLP

US PAT NO: 5,767,239 [IMAGE AVAILABLE] L1: 1 of 2

ABSTRACT:

The invention relates to a process for the preparation of cardiodilatin fragments, to highly purified cardiodilatin fragments, and to appropriate intermediates for the preparation of said fragments. Furthermore, the invention relates to highly purified cardiodilatin fragments which are free of peptide impurities and exhibit a single migration peak in capillary electrophoresis, as well as to appropriate processes for the preparation of same.

US PAT NO: 5,744,444 [IMAGE AVAILABLE] L1: 2 of 2
DATE ISSUED: Apr. 28, 1998
TITLE: HPTH-fragment-(1-37), the preparation thereof, medicaments containing same and the use thereof
INVENTOR: Wolf-Georg Forssmann, Hanover, Federal Republic of Germany
Franz Herbst, Nussloch, Federal Republic of Germany
Peter Schulz-Knappe, Neustadt, Federal Republic of Germany
Knut Adermann, Hanover, Federal Republic of Germany
Michael Gagelmann, Schriersheim, Federal Republic of Germany
ASSIGNEE: HaemoPep Pharma GmbH, Hanover, Federal Republic of Germany (foreign corp.)
APPL-NO: 08/440,117
DATE FILED: May 12, 1995
ART-UNIT: 182
PRIM-EXMR: Stephen Walsh
ASST-EXMR: Sally P. Teng
LEGAL-REP: Nikaido, Marmelstein, Murray & Oram LLP

US PAT NO: 5,744,444 [IMAGE AVAILABLE] L1: 2 of 2

ABSTRACT:

The invention relates to a peptide from human blood, designated as hPTH-(1-37), the structure of which was elucidated for the purpose of the diagnostic, medical and commercial utilization thereof. The isolation of a fragment hPTH-(38-84) proves the existence of the hPTH-(1-37). A removal of amino-terminal amino acids from the hPTH fragment-(1-37) reduces its biological activity. The hPTH-(1-37) circulating in the blood is identical with the synthetic reference substance hPTH-(1-37), however not with fragments such as hPTH-(1-33), hPTH-(1-34) or hPTH-(1-38). The molecule form hPTH-(1-37) has been proven by mass spectrometry (plasma desorption method). A different biological activity and differences in the three-dimensional peptide structure of the hPTH fragment-(1-37) in comparison to other hPTH fragments furnish evidence of that this fragment is the preferential natural peptide of the parathormone family which should be used for the treatment of diseases of the parathyroid, circulatory system, respiratory system, male genital organ and kidneys.

=> e hock, di/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	15	HOCK, CHRISTOPHER/IN
E2	USPAT	7	HOCK, DARRYL A/IN
E3	USPAT	0 -->	HOCK, DI/IN
E4	USPAT	1	HOCK, DIETER/IN
E5	USPAT	4	HOCK, DONAL D/IN
E6	USPAT	3	HOCK, DONALD E/IN
E7	USPAT	17	HOCK, FRANZ/IN
E8	USPAT	2	HOCK, FREDERICK D/IN
E9	USPAT	1	HOCK, FREDERICK RICHARD/IN
E10	USPAT	14	HOCK, FROMUND/IN
E11	USPAT	1	HOCK, GERHARD/IN
E12	USPAT	1	HOCK, HANS/IN

=> s e4

L2 1 "HOCK, DIETER"/IN

=> s l2 not l1

L3 1 L2 NOT L1

=> d leg ab

US PAT NO: 5,461,142 [IMAGE AVAILABLE] L3: 1 of 1
DATE ISSUED: Oct. 24, 1995
TITLE: Phosphorylated derivatives of cardiodilatin/ANF peptides
INVENTOR: Wolf-Georg Forssmann, Im Langgewann 93, D-6900 Heidelberg 1, Federal Republic of Germany
Michael Gagelmann, Schriesheim, Federal Republic of Germany
Dieter Hock, Neckarbischofsheim, Federal Republic of Germany
ASSIGNEE: Pharma Bissendorf Peptide GmbH, Hanover, Federal Republic of Germany (foreign corp.)
Wolf-Georg Forssmann, Heidelberg, Federal Republic of

Germany, a part interest (foreign indiv.)
APPL-NO: 08/095,049
DATE FILED: Jul. 22, 1993
ART-UNIT: 181
PRIM-EXMR: Jeffrey E. Russel
LEGAL-REP: Jacobson, Price, Holman & Stern

US PAT NO: 5,461,142 [IMAGE AVAILABLE] L3: 1 of 1

ABSTRACT:
Described are derivatives of the precursor peptide of the cardiodilatin/atrial sodiuretic factor (CDD-ANF) or fragments thereof which comprise at least the amino acid sequence of alpha-hANaP. The derivatives according to the present invention are compounds of the formula (I) ##STR1## X is a phosphate or thiophosphate group. R is NH.sub.2 or a peptide fragment from the amino acid sequence of gamma-hANaP. Radio-labelled derivatives are also possible. A method for the qualitative and/or quantitative determination of peptides containing the sequence of alpha-hANaP and a use of the compounds having the formula (I) as medicaments for various vaso- and renal related disorders are further described.

=> e magerlein/in

E#	FILE	FREQUENCY	TERM
E1	USPAT	3	MAGERLE, OTTO/IN
E2	USPAT	1	MAGERLE, RUDOLF/IN
E3	USPAT	0	--> MAGERLEIN/IN
E4	USPAT	47	MAGERLEIN, BARNEY J/IN
E5	USPAT	13	MAGERLEIN, HELMUT/IN
E6	USPAT	1	MAGERLEIN, HENDRIK/IN
E7	USPAT	1	MAGERLEIN, KAREN A/IN
E8	USPAT	1	MAGERLI, WALTER/IN
E9	USPAT	1	MAGERMAN, DAVID M/IN
E10	USPAT	1	MAGERMAN, LEONARD S/IN
E11	USPAT	2	MAGERMAN, MICHAEL L/IN
E12	USPAT	6	MAGEROWSKI, ANTHONY J/IN

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ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y

U.S. Patent & Trademark Office LOGOFF AT 14:24:54 ON 23 JUL 1998

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Last logoff: 10aug98 06:47:19
Logon file001 11aug98 12:50:16
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11aug98 12:50:31 User219511 Session D446.2
$0.00 0.107 DialUnits File410
$0.00 Estimated cost File410
$0.00 Estimated cost this search
$0.20 Estimated total session cost 0.168 DialUnits

File 155:MEDLINE(R) 1966-1998/Sep W4
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Set Items Description
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? s (pth? or hpth?) and (antibod?)

8180 PTH?
448 HPTH?
496658 ANTIBOD?
S1 481 (PTH? OR HPTH?) AND (ANTIBOD?)
? s (pth? or hpth? or (parathyroid (w) hormon?)) (10n) (antibod?)

8180 PTH?
448 HPTH?
25945 PARATHYROID
264773 HORMON?
17563 PARATHYROID(W)HORMON?
496658 ANTIBOD?
S2 377 (PTH? OR HPTH? OR (PARATHYROID (W) HORMON?)) (10N) (ANTIBOD?)
? s (pth? or hpth? or (parathyroid (w) hormon?)) (5n) (antibod?)

8180 PTH?
448 HPTH?
25945 PARATHYROID
264773 HORMON?
17563 PARATHYROID(W)HORMON?
496658 ANTIBOD?
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8180 PTH?
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25945 PARATHYROID
264773 HORMON?
17563 PARATHYROID(W)HORMON?
496658 ANTIBOD?
S4 233 (PTH? OR HPTH? OR (PARATHYROID (W) HORMON?)) (3N) (ANTIBOD?)
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448 HPTH?
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264773 HORMON?
17563 PARATHYROID(W)HORMON?
496658 ANTIBOD?
377 ((PTH? OR HPTH?) OR PARATHYROID(W)HORMON?)(10N)ANTIBOD?
1302256 ACTIV?
S5 111 ((PTH? OR HPTH? OR (PARATHYROID (W) HORMON?)) (10N) (ANTIBOD?)) AND ACTIV?
? s ((pth? or hpth? or (parathyroid (w) hormon?)) (10n) (antibod?)) (10n) activ?

8180 PTH?
448 HPTH?
25945 PARATHYROID
264773 HORMON?
17563 PARATHYROID(W)HORMON?
496658 ANTIBOD?
1302256 ACTIV?
S6 27 ((PTH? OR HPTH? OR (PARATHYROID (W) HORMON?)) (10N) (ANTIBOD?)) (10N) ACTIV?
? t s6/7/1-27;bye

6/7/1
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

09561711 98215352
Role of interleukin-6 in uncoupling of bone in vivo in a human squamous carcinoma coproducing parathyroid hormone-related peptide and interleukin-6.

Nagai Y; Yamato H; Akaogi K; Hirose K; Ueyama Y; Ikeda K; Matsumoto T; Fujita T; Ogata E
Biomedical Research Laboratories, Kureha Chemical Industry, Co., Ltd., Tokyo, Japan.
J Bone Miner Res (UNITED STATES) Apr 1998, 13 (4) p664-72, ISSN 0884-0431 Journal Code: 130
Languages: ENGLISH
Document type: JOURNAL ARTICLE
OCC tumor has been established from a human squamous carcinoma associated with humoral hypercalcemia of malignancy (HHM) and shown to overproduce parathyroid hormone-related peptide (PTHrP) and cause aggressive hypercalcemia when implanted into nude rats. In the present study, we have demonstrated by reverse transcription-polymerase chain reaction and Northern blot analysis that OCC tumor also overexpressed interleukin 6 (IL-6) mRNA and that tumor-bearing animals exhibited a marked increase in plasma IL-6 as well as %%%PTHrP%%% concentrations. When a monoclonal %%%antibody%%% against human IL-6 was injected to block the %%%activities%%% of tumor-derived IL-6, bone loss in tumor-bearing animals was significantly prevented. Quantitative bone histomorphometric analysis revealed that treatment with anti-IL-6 antibody caused a substantial decrease in both osteoclast number and eroded surface (as parameters of bone resorption) and also a significant increase in the mineral apposition rate, but little effect on the osteoblastic surface. These results provide in vivo evidence suggesting that in tumors coproducing IL-6 and PTHrP, IL-6 is involved not only in the acceleration of osteoclastic bone resorption but also, at least in part, in the suppression of osteoblastic functions in HHM syndrome.

6/7/2
DIALOG(R)File 155:MEDLINE(R)
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09539604 98221929
Involvement of prostaglandin endoperoxide H synthase-2 in osteoclast formation induced by parathyroid hormone.
Tokushima T; Sato T; Morita I; Murota S
Department of Physiological Chemistry, Graduate School, Tokyo Medical and Dental Univeristy, Japan.
Adv Exp Med Biol (UNITED STATES) 1997, 433 p307-9, ISSN 0065-2598 Journal Code: 2LU
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Prostaglandin (PG)E2 is one of the most important endogenous bone resorbing factors. In the previous study, we demonstrated that osteoclast formation induced by IL-1 beta was mediated by PGE2 produced by induced prostaglandin endoperoxide H synthase-2 (PGHS-2) in osteoclastic cells. In the same bone marrow culture system, indomethacin also suppressed the osteoclast formation induced by PTH. The inhibition was abolished by exogenously added PGE2 at dose as low as 3 x 10(-9) M, which was too low to elevate the intracellular cAMP and calcium levels and also it was too low to cause osteoclast formation by itself. In order to estimate what kind of cell produced such small amount of PGE2 in the %%%PTH%%% treatment, we carried out %%%antibody%%% staining of PGHS-1&PGHS-2 and PGHS %%%activity%%% in the intact bone marrow cells. PTH was found to induce PGHS activity in tartrate-resistant acid phosphatase (TRACP) positive mononuclear cells and the PGHS activity was inhibited by NS-398, a specific inhibitor of PGHS-2. Immunocytochemical staining supported the expression of PGHS-2 in TRACP-positive mononuclear cells. These findings suggest that PGHS-2 induced by PTH may regulate osteoclast formation by different mechanism from that induced by IL-1 beta.

6/7/3
DIALOG(R)File 155:MEDLINE(R)
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09083480 97330995
Parathyroid hormone exerts disparate effects on osteoblast differentiation depending on exposure time in rat osteoblastic cells.
Ishizuya T; Yokose S; Hori M; Noda T; Suda T; Yoshiki S; Yamaguchi A
Department of Oral Pathology, School of Dentistry, Showa University, Tokyo 142, Japan.
J Clin Invest (UNITED STATES) Jun 15 1997, 99 (12) p2961-70, ISSN 0021-9738 Journal Code: HS7
Languages: ENGLISH
Document type: JOURNAL ARTICLE
It has been reported that PTH exerts bone-forming effects in vivo when administered intermittently. In the present study, the anabolic effects of PTH(1-34) on osteoblast differentiation were examined in vitro. Osteoblastic cells isolated from newborn rat calvaria were cyclically treated with PTH(1-34) for the first few hours of each 48-h incubation cycle. When osteoblastic cells were intermittently exposed to PTH only for the first hour of each 48-h incubation cycle and cultured for the remainder of the cycle without the hormone, osteoblast differentiation was inhibited by suppressing alkaline phosphatase activity, bone nodule formation, and mRNA expression of alkaline phosphatase, osteocalcin, and PTH/PTHrP receptor. Experiments using inhibitors and stimulators of cAMP/protein kinase A (PKA) and Ca2+/PKC demonstrated that cAMP/PKA was the major signal transduction system in the inhibitory action of PTH. In contrast, the

intermittent exposure to PTH for the first 6 h of each 48-h cycle stimulated osteoblast differentiation. Both cAMP/ PKA and Ca2+/PKC systems appeared to be involved cooperatively in this anabolic effect. Continuous exposure to PTH during the 48-h incubation cycle strongly inhibited osteoblast differentiation. Although both cAMP/PKA and Ca2+/PKC were involved in the effect of continuous exposure to %%%PTH%%%, they appeared to act independently. A neutralizing %%%antibody%%% against IGF-I blocked the stimulatory effect on alkaline phosphatase %%%activity%%% and the expression of osteocalcin mRNA induced by the 6-h intermittent exposure. The inhibitory effect induced by the 1-h intermittent exposure was not affected by anti-IGF-I antibody. These results suggest that PTH has diverse effects on osteoblast differentiation depending on the exposure time in vitro mediated through different signal transduction systems. These in vitro findings explain at least in part the in vivo action of PTH that varies with the mode of administration.

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DIALOG(R)File 155:MEDLINE(R)
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08996464 97193975
Antibody against synthetic rat PTH peptide (1-34) blocks PTH-mediated cAMP formation and phosphate transport in opossum kidney cells.
Zhang Z; Raj HG; Reddy RL; Baliga R
Department of Pediatrics, University of Mississippi Medical Center, Jackson 39216, USA.
Nephron (SWITZERLAND) 1997, 75 (2) p245-8, ISSN 0028-2766 Journal Code: NW8
Contract/Grant No.: SO-RR-5376, RR, NCRR
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A novel antibody against synthetic rat parathyroid hormone (rPTH(1-34)) was successfully produced in rabbits at a titer of 1:3,000. The ability of this antibody to block PTH was studied utilizing the hormone-sensitive cAMP formation and Na(+)-dependent phosphate transport in the opossum kidney (OK) cells. rPTH peptide(1-34) stimulated cAMP formation and inhibited Na(+)-dependent phosphate transport in OK cells in a dose-dependent manner. Treatment of OK cells with the antisera significantly decreased the level of cAMP and attenuated the inhibition of Na(+)-dependent phosphate transport in response to rPTH(1-34) at a dilution of 1:1,000. Nonimmune rabbit sera at the same dilution did not influence these hormone-sensitive effects. We conclude that %%%antibody%%% against synthetic %%%PTH%%% peptide can be used to study the biological %%%activities%%% of this hormone.

6/7/5
DIALOG(R)File 155:MEDLINE(R)
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08359718 95342320
Parathyroid hormone and the cellular immune system.
Shurtz-Swirski R; Shkolnik T; Shasha SM
Renal Unit, Western Galilee Hospital, Nahariya, Israel.
Nephron (SWITZERLAND) 1995, 70 (1) p21-4, ISSN 0028-2766 Journal Code: NW8
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
Parathyroid hormone (PTH) is the main hormone controlling calcium concentration in the extracellular fluid (ECF) through its biological activity on bone, kidney and intestine. However, data published over the last two decades indicate that PTH may act as an immunomodulator. The purpose of the present review is to summarize the effects of PTH on various immune functions. Polymorphonuclear leukocytes of patients with chronic renal failure (CRF) and elevated blood levels of PTH showed impaired migration, reduced phagocytic and bactericidal %%%activity%%%, and inhibited granulocyte chemotaxis. %%%Antibody%%% production and T and B lymphocyte proliferation are affected by %%%PTH%%%, both in vivo and in vitro. Possible implications of the involvement of PTH and its fragments in CRF are discussed. (36 Refs.)

6/7/6
DIALOG(R)File 155:MEDLINE(R)
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08270376 95203246
Involvement of cell cycle and mitogen-activated pathways in induction of parathyroid hormone-related protein gene expression in rat aortic smooth muscle cells.
Okano K; Pirola CJ; Wang HM; Forrester JS; Fagin JA; Clemens TL
Department of Medicine, Cedars-Sinai Research Institute, Cedars-Sinai Medical Center, University of California-Los Angeles School of Medicine 90048.
Endocrinology (UNITED STATES) Apr 1995, 136 (4) p1782-9, ISSN 0013-7227 Journal Code: EGZ
Contract/Grant No.: HL-47811, HL, NHLBI; DK-42792, DK, NIDDK; HL-43802, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
PTH-related protein (PTHrP) is induced in aortic vascular smooth muscle cells (VSMC) in association with mitogen-stimulated proliferation. In this study we examined the role of the cell cycle in the control of PTHrP gene expression. In asynchronously cycling cells grown in serum-containing medium, PTHrP-immunoreactive cells were enriched in G2+M, as revealed by fluorescence-%%%activated%%% cell sorting using a specific monoclonal %%%antibody%%%. %%%PTHrP%%% messenger RNA (mRNA) increased transiently in
cells after release from chemically induced cell cycle blockade; levels increased by 10-fold at 2 h, coincident with expression of histone-4 mRNA and enrichment of VSMC in the early S phase. However, PTHrP mRNA levels then declined abruptly while the proportion of cells in the S phase and histone-4 mRNA levels remained constant for 8 h. When cell cycle-arrested cells were exposed to fresh serum-containing medium, angiotensin-II, or phorbol ester without removing the cell cycle blocking agents, PTHrP mRNA levels were induced over a time course identical to that observed in cells released from the blockade. This suggests that progression through the cycle per se is not necessary for mitogen-induced PTHrP mRNA expression, and that conventional chemical synchronization is not adequate to examine the cell cycle dependency of PTHrP mRNA abundance in VSMC. By contrast, in two different PTHrP-producing carcinoma cell lines, PTHrP and its mRNA were not altered as a function of cell cycle, demonstrating that different mechanisms control PTHrP expression in these cancer cells. In conclusion, constitutive immunoreactive levels of PTHrP are low in normally cycling VSMC (but not cancer cells) and accumulate during the latter stages of the cell cycle, suggesting a role for this protein in the process of smooth muscle cell division. However, separate mechanisms, which are independent of cell cycle, operate through a protein kinase-C-dependent pathway(s) to mediate the stimulation of PTHrP gene expression by vasoconstrictors such as angiotensin-II.

6/7/7
DIALOG(R)File 155:MEDLINE(R)
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07826786 93155038
Gs mediates hormonal inhibition of the calcium pump in liver plasma membranes.
Jouneaux C; Audigier Y; Goldsmith P; Pecker F; Lotersztajn S
Institut National de la Sante et de la Recherche Medicale Unite 99, Hopital Henri Mondor, Creteil, France.
J Biol Chem (UNITED STATES) Feb 5 1993, 268 (4) p2368-72, ISSN 0021-9258 Journal Code: HIV
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have reported that the calcium pump in liver plasma membranes is coupled to Gs or a Gs-like protein. However, we show here that isoproterenol, which activated adenylyl cyclase via Gs, had no effect on the calcium pump, while human calcitonin, human parathyroid hormone, and mini-glucagon, which inhibited this system, did not affect adenylyl cyclase activity. In order to determine the nature of the G protein coupled to the calcium pump, we used the RM antibody, raised against the carboxyl-terminal decapeptide of Gs alpha, which antagonized adenylyl cyclase %%%activation%%% by isoproterenol or glucagon. The RM %%%antibody%%% specifically blocked calcium pump inhibition by mini-glucagon, calcitonin, or %%%parathyroid%%% %%%hormone%%%, while it did not affect guanosine 5'-O-(thiotriphosphate) inhibition. Its effect was mimicked by the corresponding decapeptide RMHLRQYELL. The AS/7 antibody, reactive with Gt alpha, Gi 1 alpha, and Gi2 alpha, was ineffective. Complementation of liver plasma membranes with in vitro translated Gs alpha-2, the large form of Gs alpha, led to a 40% decrease in calcium pump activity, with a parallel 2-fold increase in adenylyl cyclase activity. In vitro translated Gi1 alpha did not affect the calcium pump activity, while it evoked a 40% inhibition of adenylyl cyclase activity. We conclude that a same Gs alpha may be coupled either to the calcium pump or to adenylyl cyclase. However, Gs is functionally specialized, since it does not ensure cross-talk between the two receptor-effector systems. These results point out the possible compartmentalization of Gs.

6/7/8
DIALOG(R)File 155:MEDLINE(R)
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07448771 92248391
PTH stimulates the proliferation of TE-85 human osteosarcoma cells by a mechanism not involving either increased cAMP or increased secretion of IGF-I, IGF-II or TGF beta.
Finkelman RD; Mohan S; Linkhart TA; Abraham SM; Boussy JP; Baylink DJ
Department of Periodontics, Loma Linda University, CA.
Bone Miner (NETHERLANDS) Feb 1992, 16 (2) p89-100, ISSN 0169-6009 Journal Code: BMI
Contract/Grant No.: AR 31062, AR, NIAMS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Injections of parathyroid hormone (PTH) result in increased bone formation in several species. Work in our laboratory and others has shown a stimulation of bone cell proliferation and growth factor production by PTH.

Our purpose was to study the effects of PTH on a human bone cell line using TE-85 human osteosarcoma cells as a model. After 24 h treatment, PTH caused an increase in cell proliferation as measured by cell counts and [3H]-thymidine incorporation. Proliferation was not inhibited by an anti-transforming growth factor beta (TGF beta) %%%antibody%%% which could abolish stimulation by exogenous TGF beta. %%%PTH%%% did not stimulate cAMP production, alkaline phosphatase %%%activity%%% or production of insulin-like growth factors I or II (IGF-I or IGF-II) in TE-85 cells. Although basal TE-85 proliferation was slowed by incubation with the calcium channel blocking agent verapamil, PTH still caused an increase in growth rate. We conclude that PTH directly stimulates TE-85 proliferation via a mechanism not involving increased adenylate cyclase activity or increased secretion of IGF-I, IGF-II or TGF beta and may stimulate bone formation in vivo by activating some other mitogenic signal to increase bone cell proliferation.

6/7/9
DIALOG(R)File 155:MEDLINE(R)

07444265 92180698
Tissue and urokinase plasminogen activators in bone tissue and their regulation by parathyroid hormone.
Leloup G; Peeters-Joris C; Delaisse JM; Opdenakker G; Vaes G
Laboratoire de Chimie Physiologique (Connective Tissue Group), Universite de Louvain, Belgium.
J Bone Miner Res (UNITED STATES) Oct 1991, 6 (10) p1081-90, ISSN 0884-0431 Journal Code: 130
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The identification of the plasminogen activator (PA) types present in bone and the regulation of their activity by parathyroid hormone (PTH) were investigated in cultures of fetal mouse calvariae with the use of either a chromogenic substrate or a zymographic assay. PA was detected essentially in the tissue extracts of the explanted bones, with only 1-2% of the total activity released in the surrounding culture media. From their electrophoretic behavior compared to PAs of other mouse tissues and from their response to a specific antibody raised against the tissue type PA (tPA), two major molecular species, of 70 and 48 kD were identified as tPA and urokinase (uPA), respectively, a third minor species of 105 kD being likely to correspond to complexes between tPA and an inhibitor; the culture fluids, moreover, contained enzymatically active degradation products of uPA of 42 and 29 kD. The PA activity of the bone extracts was only minimally affected by the addition of fibrinogen fragments to the chromogenic assays. PTH induced bone resorption and stimulated in parallel the accumulation of PA in the tissue; other bone-resorbing agents, 1,25-dihydroxyvitamin D3 and prostaglandin E2, had similar effects. Densitometric scanning of the zymograms of the bone extracts indicated that PTH stimulated only the production of tPA and had no effect on that of uPA. However, PTH also enhanced the release of uPA (both the 48 kD and the 29 kD forms) from the bones into the media. Although inhibiting bone resorption, calcitonin had no effect on the PTH-induced accumulation of PA in bone or on the release of tPA, but it prevented the PTH-induced accumulation of 29 kD uPA in the culture fluids. Thus these studies support the view that tPA and possibly also uPA may have a role in the physiology of bone; the nature of this role remains to be elucidated, however.

6/7/10
DIALOG(R)File 155:MEDLINE(R)

07423131 91257767
Osteolytic activity of Walker carcinosarcoma 256 is due to parathyroid hormone-related protein (PTHrP).
Scharla SH; Minne HW; Lempert UG; Krieg P; Rappel S; Maurer E; Grohe U; Ziegler R
Abteilung Innere Medizin I, Endokrinologie und Stoffwechsel, Klinikum der Universitat Heidelberg, Germany.
Horm Metab Res (GERMANY) Feb 1991, 23 (2) p66-9, ISSN 0018-5043 Journal Code: GBD
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The hypercalcemic Walker carcinosarcoma 256 of the rat is an animal model for humoral hypercalcemia of malignancy. Previous in vivo studies suggested the production of a parathyroid hormone-related protein (PTHrP) by the Walker tumor. Therefore, we have measured immunoreactive PTHrP in serum-free conditioned medium from cells derived from this tumor using an antibody raised against human PTHrP(1-34). Walker tumor cell conditioned medium (WCM) displaced 125I-hPTHrP(1-34) from the antibody in a dose dependent manner, whereas control medium contained no immunoreactive PTHrP. In contrast, we detected no secretion of immunoreactive rat parathyroid hormone (rat PTH) by the Walker tumor cells using a midregional radioimmunoassay for rat PTH. WCM stimulated adenylate cyclase in osteoblast like cells, the dose-response curve paralleling that of hPTHrP(1-34). This effect could be inhibited by the PTH antagonist (8Nle, 18Nle, 34Tyr)bPTH(3-34) and by the addition of anti-%%%hPTHrP%%%(1-34) %%%antibody%%%. Bone resorbing %%%activity%%% of WCM in organ culture (calvaria of fetal rats) was not inhibited by indomethacin and glucocorticoids, suggesting a prostaglandin independent mechanism of osteoclast activation in this model.

6/7/11
DIALOG(R)File 155:MEDLINE(R)

07404918 90372128
Release of parathyroid hormonelike peptides by fetal rat long bones in culture.
Bergmann P; Nijs-De Wolf N; Pepersack T; Corvilain J
Department of Clinical Chemistry, Hopital Universitaire Brugmann, Universite Libre de Bruxelles, Belgium.
J Bone Miner Res (UNITED STATES) Jul 1990, 5 (7) p741-53, ISSN 0884-0431 Journal Code: 130
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We observed that culture medium conditioned with fetal rat long bones stimulated cyclic AMP production by canine renal cortical membranes. This cyclase-stimulating activity (CSA) was retained by an ultrafiltration membrane with a molecular weight cutoff of 5000; three biologically active peaks with an approximate molecular weight of 18,000-25,000, 9000-12,000, and 4000-6000 were separated by high-performance liquid chromatography. The biologic activity was destroyed by trypsin digestion. The stimulation of adenylate cyclase by the medium and by the three peaks was inhibited by [N-leu8,18,Tyr34]parathyroid hormone-(3-34)-amide and by [Tyr34]parathyroid hormone-(7-34)amide. Preincubation of the bone culture medium and of the three peaks with an %%%antibody%%% raised against human %%%parathyroid%%% %%%hormone%%%-(1-34) did not decrease the biologic %%%activity%%% more than incubation with nonimmune serum. However, the biologic activity of the three active peaks was significantly suppressed after preincubation with an antiserum directed against the N-terminal region of the parathyroid hormone-related peptide of malignancy. The release of CSA into the bone culture medium was enhanced by parathyroid hormone induction and by 1,25-dihydroxycholecalciferol. It was decreased by calcitonin. We conclude that fetal murine bones in culture release peptides that stimulate the adenylate cyclase of renal cortical membranes. These peptides are antigenically similar to the parathyroid hormone-related peptide of malignancy. Their release from bones is modulated by hormones that control bone resorption.

6/7/12
DIALOG(R)File 155:MEDLINE(R)

07364405 91193551
Production and characterisation of monoclonal antibodies to parathyroid hormone (1-34).
Logue FC; Perry B; Biggart EM; Chapman RS; Beastall GH
Institute of Biochemistry, Royal Infirmary, Glasgow, U.K.
J Immunol Methods (NETHERLANDS) Mar 21 1991, 137 (2) p159-66, ISSN 0022-1759 Journal Code: IFE
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Monoclonal %%%antibodies%%% to the biologically %%%active%%% N terminal region of %%%parathyroid%%% %%%hormone%%% (%%%PTH%%%) suitable for use in
the measurement of circulating PTH concentrations have proved difficult to produce. In this study, no serum PTH antibody titres could be detected in mice using synthetic human PTH (1-34) (free or coupled to albumin) or PTH (1-10) (coupled to keyhole limpet haemocyanin) as immunogen. A consistent response to PTH (1-34) peptide was obtained in DA rats. We have produced five monoclonal antibodies to PTH (1-34) derived from the fusion of DA rat spleen cells and the mouse myeloma line X63 Ag.8.653. Bulk production of the antibodies was achieved using congenitally athymic mice for ascites production. Antibody assessment studies revealed the antibodies to be sensitive to the oxidation state of the methionine residues in PTH (1-34). Two of the antibodies, 3B3 and 6E3, were shown to be of potential use in measuring circulating PTH (1-84) when used in combination with available antibodies to C terminal PTH. A third antibody, 4G3, which failed to recognise PTH (1-84) when used in combination with 3B3, formed the basis of a specific assay for PTH (1-34).

6/7/13
DIALOG(R)File 155:MEDLINE(R)

07246547 93124754
[Immunohistochemical classification and ultrastructural study of hyperparathyroidism]
Takada M
Department of Urology, Kinki University School of Medicine.
Nippon Hinyokika Gakkai Zasshi (JAPAN) Nov 1992, 83 (11) p1767-73, ISSN 0021-5287 Journal Code: KRB
Languages: JAPANESE Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE English Abstract
Immunohistochemical and ultrastructural studies were performed on cases

with hyperparathyroidism. The relationship between histology and cell activity in hyperfunctioning parathyroid glands was studied. Furthermore, the synthesis-secretion process of parathyroid hormone (PTH), which has been more or less elucidated biochemically, was studies by a morphological means. The subjects employed in the present study were 23 cases of primary hyperparathyroidism (PHPT) and 31 cases of secondary hyperparathyroidism (SHPT). Based on the results of the immunohistochemical study using anti-PTH antibody, the histology of the parathyroid gland was classified into 4 types: type A; sporadic cells showing intense yellowish brown staining in their cytoplasm, type B; glandular cells showing intense yellowish brown staining specifically in their cytoplasm, type C; as a whole the cells were weakly stained, but intensely stained cells were absent, and type D; only the cytoplasm of large cells showed uniform and intense yellowish brown staining. In both PHPT and SHPT, type C constituted about 80%. On the other hand, all water clear cell hyperplasia in SHPT showed type D staining. Electron microscopic studies performed on the hyperparathyroidism revealed that the rough endoplasmic reticulum and Golgi apparatus, which are related to the synthesis of PTH, were well developed. Immunoelectron microscopy revealed that only the secretory granules were specifically stained with the anti-%%%PTH%%% %%%antibody%%%. This finding suggests that %%%PTH%%% becomes %%%active%%% once it reaches the secretory granule.

6/7/14
DIALOG(R)File 155:MEDLINE(R)
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07010787 92108959
Immunoassays for parathyroid hormone 1-84 in the diagnosis of hyperparathyroidism.
Nussbaum SR; Potts JT Jr
Medical Services and Endocrine Unit, Massachusetts General Hospital, Boston.
J Bone Miner Res (UNITED STATES) Oct 1991, 6 Suppl 2 pS43-50; discussion S61, ISSN 0884-0431 Journal Code: 130
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
The two most frequent causes for hypercalcemia are primary hyperparathyroidism and hypercalcemia associated with malignancy. Elevated or inappropriately high PTH serum levels are the hallmark of hyperparathyroidism. Sensitive immunometric assays for the secreted, biologically %%%active%%%, intact %%%parathyroid%%% %%%hormone%%% molecule,
%%%PTH%%%-(1-84), employ two populations of region-specific %%%antibodies%%%, take advantage of saturation kinetics rather than competitive binding, and have many technical advantages over conventional radioimmunoassay. Approximately 90% of patients with primary hyperparathyroidism have elevated serum levels of PTH-(1-84) by immunometric assay; the remainder have inappropriately elevated values of PTH for the serum calcium concentration. Clinical correlation studies comparing measurements of PTH using antisera that recognize the carboxyl, midregion, or amino terminus of PTH with PTH levels determined by immunometric assays demonstrate elevated values in equivalent numbers of hyperparathyroid individuals. Immunometric assays for PTH-(1-84) have their greatest value in separating patients with hyperparathyroidism from those with hypercalcemia of malignancy. In earlier studies using region-specific antisera, there was virtually always an overlap of serum PTH levels in hyperparathyroidism and hypercalcemia associated with malignancy. In contrast, analysis of results using PTH-(1-84) immunometric assays in several hundred reported patients shows a complete separation of PTH values. Clinical judgment, combined with measurement of PTH in the setting of hypercalcemia, can lead to the diagnosis of hyperparathyroidism with confidence in essentially all patients. (19 Refs.)

6/7/15
DIALOG(R)File 155:MEDLINE(R)
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06609507 90091984
Insulin antagonistic effects of insulin receptor antibodies on plasma membrane (Ca2+ + Mg2+) ATPase activity: a possible etiology of type B insulin resistance.
Nagy K; Grunberger G; Levy J
Department of Internal Medicine, Wayne State University School of Medicine, Detroit, Michigan 48201.
Endocrinology (UNITED STATES) Jan 1990, 126 (1) p45-52, ISSN 0013-7227 Journal Code: EGZ
Contract/Grant No.: SO7-RR-05384, RR, NCRR
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The regulatory effect of insulin on plasma membrane (Ca2+ + Mg2+)ATPase activity in target tissues for insulin was proposed to be of importance in mediating the hormone's cellular action. Consequently, polyclonal insulin receptor antibodies from patients with type B insulin resistance (B7 and B10) were used as probes to further explore a possible role for this ATPase in insulin action. The antibodies B7 and B10 obtained during the active phase of the disease manifested insulinomimetic actions in rat renal cortical basolateral membranes by displacing [125I]insulin bound to the membranes and stimulating the tyrosine kinase activity of solubilized insulin receptors in a dose-dependent manner. In contrast, these antibodies had insulin antagonistic effects on the membrane (Ca2+ + Mg2+)ATPase activity. While insulin stimulated, both antibodies inhibited the ATPase basal activity in a dose-dependent manner. Furthermore, the stimulatory effect of insulin on the ATPase was completely abolished by the antibodies. Immunoglobulin fractions obtained from patient B10 in the clinically inactive phase of the disease and from pooled normal human sera did not affect basal or insulin-stimulated ATPase activity. The effects of insulin receptor antibodies on basal and insulin-stimulated (Ca2+ + Mg2+)ATPase %%%activities%%% were specific. The receptor %%%antibody%%% did not affect %%%PTH%%%-stimulated (Ca2+ + Mg2+) ATPase %%%activity%%%, nor did it affect other kidney basolateral membrane ATPase basal activities. The data reveal that insulin receptor antibodies have a direct regulatory effect on the plasma membrane (Ca2+ + Mg2+) ATPase. We suggest that the insulin antagonistic effects of the insulin receptor antibodies on the ATPase might explain in part the impaired insulin action in type B insulin resistance.

6/7/16
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06276573 87166579
Transient hypoparathyroidism induced by synthetic human parathyroid hormone-(1-34) treatment.
Audran M; Basle MF; Defontaine A; Jallet P; Bidet MT; Ermias A; Tanguy G; Pouplard A; Reeve J; Zanelli J; et al
J Clin Endocrinol Metab (UNITED STATES) May 1987, 64 (5) p937-43, ISSN 0021-972X Journal Code: HRB
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Daily injections of low doses of a synthetic fragment of human PTH [hPTH-(1-34) have increased iliac trabecular bone volume when used in the treatment of osteoporosis. In approximately 50 patients no major side-effects had occurred. However, during daily sc 100-micrograms injections of the peptide, one patient repeatedly developed parathyroid hypofunction which resolved each time treatment was stopped. Specific immunoglobulin G (IgG) antibodies binding [125I]hPTH-(1-34) were identified in the patient's serum, and positive immunohistochemical reactions were obtained when bovine parathyroid sections were exposed to the patient's IgG. After adsorption with PTH, the patient's IgG, free of anti-PTH antibodies, reacted with renal cell membranes, as demonstrated by indirect immunofluorescence and blocked renal PTH-dependent adenylate-cyclase %%%activation%%% in vitro. These results support the hypothesis that anti-%%%PTH%%% receptor as well as anti-%%%PTH%%% %%%antibodies%%% were
generated during %%%hPTH%%%-(1-34) treatment, which led to the development of hypoparathyroidism when their titers were high.

6/7/17
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06243542 85258588
Identification of a monoclonal antibody which interacts with the parathyroid hormone receptor-adenylate cyclase system in murine bone.
Weinshank RL; Cain CD; Vasquez NP; Luben RA
Mol Cell Endocrinol (NETHERLANDS) Jul 1985, 41 (2-3) p237-46, ISSN 0303-7207 Journal Code: E69
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We have produced monoclonal antibodies which bind specifically to mouse bone cells and then selected these monoclonal antibodies for their ability to inhibit parathyroid hormone (PTH) responses in mouse cranial bone treated with the (1-34) amino terminal peptide of bovine PTH [bPTH(1-34)]. One clone, designated 3-6, characterized as an IgM(kappa), significantly inhibited the accumulation of cAMP in response to bPTH(1-34) at concentrations of hormone between 10(-9) and 10(-7) M. This antibody was subsequently isolated by gel filtration and shown to bind to intact mouse calvariae, with saturation binding occurring at 3 micrograms/ml IgM. A maximal inhibition of approximately 70% of the cAMP accumulation produced in response to 2.5 X 10(-9) M (100 ng/ml) bPTH(1-34) was obtained with 7 micrograms/ml of the purified 3-6 IgM. At this concentration of 3-6 IgM, the half-maximal dose of PTH for activation of cAMP accumulation was increased from 5 X 10(-9) M to 2 X 10(-8) M with no reduction in maximal levels of cAMP production. The utility of this antibody as an inhibitor was further tested by its ability to block the binding of an iodinated PTH analogue, 125I-[Nle8, Nle18, Tyr34]-bPTH(1-34) to mouse cranial bone. The 3-6 IgM at a concentration of 5 X 10(-8) M inhibited 70% of the specific binding of the 125I-labeled analogue. In the absence of parathyroid hormone, 2 X 10(-8) M 3-6 IgM produced a 4-fold increase in cAMP above basal levels, as compared to 40-fold maximal increases observed with %%%PTH%%%, indicating a partial %%%PTH%%% agonist %%%activity%%% of this
%%%antibody%%%. When tested for effects on other hormones, 3-6 IgM did not inhibit cAMP accumulation produced in response to salmon calcitonin, epinephrine, prostaglandin E2 or cholera toxin. We propose that the 3-6 monoclonal IgM is specific for the PTH receptor or a component of the PTH

receptor-adenylate cyclase system and that this or similar antibodies will serve as useful reagents for future molecular characterization of this receptor.

6/7/18
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06210914 87306589
Monoclonal antibodies to human parathyroid hormone (1-34) and their use in the immunocytochemical detection of parathyroid tumours.
Moharned IA; Hubbard R; Ah-Sing E; Chakraborty J
Hybridoma (UNITED STATES) Aug 1987, 6 (4) p381-7, ISSN 0272-457X Journal Code: GFS
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Monoclonal %%%antibodies%%% against the biologically %%%active%%% N-terminal fragment of human %%%parathyroid%%% %%%hormone%%%, hPTH (1-34),
were produced. The procedure included the use of novel secondary immunization in vitro of mouse spleen cell cultures. Dissociated spleen cells from primary immunized Balb/c mice, were cultured for five days in the presence of thymocyte conditioned media (TCM) and synthetic hPTH (1-34). Contrary to previous findings by other workers, in our hands Balb/c mice responded well. Following immunization the spleen cells were fused with NSI myeloma cells and cultured for eleven days before screening for antibody. Using an enzyme linked immunosorbent assay (ELISA) a number of positive clones were detected. Positive cells were cloned by limiting dilution and fifteen specific monoclonal hybridomas were produced. The immunoglobulin class of the different monoclonal antibodies was found to be IgGl. The immunocytochemical reaction was tested with chief cell carcinoma tissue and found to be clearly positive.

6/7/19
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06135203 88025210
Parathyroid hormone induction of creatine kinase activity and DNA synthesis is mimicked by phospholipase C, diacylglycerol and phorbol ester.
Somjen D; Zor U; Kaye AM; Harell A; Binderman I
Hard Tissues Unit, Ichilov Hospital, Tel Aviv Medical Center, Israel.
Biochim Biophys Acta (NETHERLANDS) Nov 12 1987, 931 (2) p215-23, ISSN 0006-3002 Journal Code: A0W
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Parathyroid hormone (PTH), which increases cAMP levels, also induces an increase in the activity of the brain isozyme of creatine kinase and in DNA synthesis in osteoblast-enriched bone cell cultures by a cAMP-independent mechanism. The following results lead us to the conclusion that PTH induction of brain isozyme of creatine kinase activity and DNA synthesis occurs by activation of membranal phospholipid metabolism leading to increased protein kinase C activity and Ca2+ mobilization, a mechanism demonstrated for several growth factors and other hormones. (1) Binding of membranal phospholipids by agents such as gentamycin or antiphospholipid %%%antibodies%%% abolishes the stimulation by %%%PTH%%% of creatine kinase %%%activity%%% and DNA synthesis but not of cAMP production. (2) Treatment of cell cultures with exogenous phospholipase C increases brain isozyme of creatine kinase activity and DNA synthesis, but not cAMP production; these stimulations are also blocked by serum containing anti-phospholipid %%%antibodies%%%. %%%PTH%%% has no additional effect on stimulation of creatine kinase %%%activity%%% by phospholipase C (and only a slight effect on DNA synthesis). (3) A synthetic diacylglycerol (1-oleyl-2-acetyl glycerol) or phorbol ester (phorbol 12-myristate 13-acetate) or Ca2+ ionophore, A23187 induces creatine kinase activity and DNA synthesis in the cultures. However, this effect is not blocked by antiphospholipid sera and PTH has no additional effect. (4) Inhibition of protein kinase C activity by drugs reported to inhibit the enzyme (retinoic acid, quercetin) abolishes the stimulation of brain isozyme of creatine kinase activity and of DNA synthesis by PTH.

6/7/20
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05823414 90069831
Bovine parathyroid tissue: a model to compare the biosynthesis and secretion of parathyroid hormone and parathyroid hormone-related peptide.
Connor CS; Drees BM; Thurston A; Forte L; Herrmreck AS; Hamilton JW
Department of Surgery, Leavenworth Veterans Administration Medical Center, Kan. 66048.
Surgery (UNITED STATES) Dec 1989, 106 (6) p1057-62, ISSN 0039-6060 Journal Code: VC3
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Bovine parathyroid tissue was evaluated as a model to compare parathyroid hormone-related peptide (PTH-rP) and parathyroid hormone (PTH) secretion. Tissue was incubated in variable calcium levels (n = 5). A parathyroid cell digest was prepared from collagenase-treated glands. PTH-rP and PTH levels were determined by radioimmunoassay. PTH-rP bioactivity was determined by 3H-cAMP production in a UMR 106 cell bioassay. PTH-rP levels in the incubation medium were 2.0 ng/mg protein (0.25 mmol Ca++), 2.2 ng/mg protein (1.25 mmol Ca++), and 1.9 ng/mg protein (2.5 mmol/L Ca++). PTH levels were 321 ng/mg protein (0.25 mmol/L Ca++) and 200 ng/mg protein (2.5 mmol Ca++). Therefore, calcium significantly inhibited PTH but not PTH-rP secretion ($p = 0.03$). Addition of incubation medium to the bioassay resulted in 3H-cAMP levels that were 8 to 10 times greater than basal levels. Greater than 50% of the %%%activity%%% persisted after addition of %%%PTH%%% %%%antibody%%%, demonstrating that a significant amount of the %%%activity%%% was caused by PTH-rP. Tissue PTH-rP was 5.1 ng/mg protein, compared with 2080 ng/mg protein for PTH. We conclude that (1) bovine parathyroid tissue contains bioactive PTH-rP and is a useful model to compare the biosynthesis and secretion of PTH-rP and PTH in normal tissue and (2) unlike PTH, PTH-rP secretion is not regulated by calcium.

6/7/21
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05707701 89107076
Osteoblast-like cells secrete granulocyte-macrophage colony-stimulating factor in response to parathyroid hormone and lipopolysaccharide.
Weir EC; Insogna KL; Horowitz MC
Section of Comparative Medicine, Yale University School of Medicine, New Haven, Connecticut 06510.
Endocrinology (UNITED STATES) Feb 1989, 124 (2) p899-904, ISSN 0013-7227 Journal Code: EGZ
Contract/Grant No.: AM-30102, AM, NIADDK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The cellular mechanism by which PTH and other osteotropic substances stimulate bone resorption is unclear. One hypothesis is that PTH-stimulated osteoblasts release cytokines which activate osteoclasts or osteoclast precursors. To examine whether cytokines are released by osteoblast-like cells in vitro, medium conditioned by a clonal rat osteosarcoma cell line 17/2.8 (ROS) was examined for mitogenic activity using a helper T lymphocyte line HT-2. This line proliferates in response to interleukin-2 (IL-2), IL-4, and granulocyte-macrophage colony-stimulating factor (GM CSF). Conditioned medium (CM) from untreated ROS cells caused proliferation of HT-2 cells. Treatment of ROS cells with PTH or lipopolysaccharide (LPS) caused a dose-dependent increase in the secretion of this mitogenic activity. To further define the nature of this mitogenic activity, we examined the effect of incubation of CM with neutralizing antibodies to IL-2, IL-4, and GM CSF. Mitogenic activity induced by both PTH- and LPS-treated ROS cell CM was completely inhibited by anti-GM CSF antibody, whereas there was no reduction in %%%activity%%% in the presence of %%%antibodies%%% to IL-2 or IL-4. Partial purification of both %%%PTH%%%- and LPS-treated CM using reverse phase HPLC resulted in a single peak of HT-2 mitogenic activity, which in both cases was completely inhibited by anti-GM CSF %%%antibody%%%. These findings suggest that %%%PTH%%%- and LPS-treated ROS cells secrete a T cell mitogenic %%%activity%%% which, by functional, serological, and biochemical criteria, is indistinguishable from GM CSF.

6/7/22
DIALOG(R)File 155:MEDLINE(R)
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05613281 89380749
Pulse amplitude and frequency modulation of parathyroid hormone in plasma.
Harms HM; Kaptaina U; Kulpmann WR; Brabant G; Hesch RD
Abteilung Klinische Endokrinologie im Zentrum Innere Medizin, Hannover, West Germany.
J Clin Endocrinol Metab (UNITED STATES) Oct 1989, 69 (4) p843-51, ISSN 0021-972X Journal Code: HRB
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Inconclusive reports on pulsatile secretion of PTH in man have been published. In this study PTH was measured by intact and PTH-(44-68) assays. Central venous blood sampling was performed every 2 min in 10 healthy men between 6-9 h and in 3 male patients with osteoporosis for over 6 h. Pulsatile PTH secretion was identified for healthy men and controls. Narrow pulses and bursts of narrow pulses (broad pulse) could be distinguished. Six narrow pulses per h with 26 +/- 16 ng/L amplitude and 1 burst of narrow pulses/h were detected for the intact hormone. One narrow pulse/h with 25 +/- 12 ng/L amplitude and 1 burst of narrow pulses (broad pulse) every 2 h were found (Pulsar) for PTH-(44-68). Intact and PTH-(44-68) exhibit in part a concordant pattern. Results from 3 patients with osteoporosis show a decreased amplitude and frequency of pulsatile PTH secretion. The same decreased pattern was demonstrated in a postmenopausal osteoporotic woman. A constant decline in ionized calcium elicits major secretory episodes of PTH, and ionized calcium increases after major secretory episodes of PTH. We conclude that pulsatile secretion of PTH in healthy young men is the physiological mode of secretion. Low pulsatile secretion of PTH might be

related to low turnover osteoporosis.

6/7/23
DIALOG(R)File 155:MEDLINE(R)

05402515 89018059
[Basic studies on an immunoradiometric assay system for human parathyrin (intact PTH1-84)]
Kanao K; Honda M; Ishihara S; Moriuma H; Mishima T; Tomonobu M; Usami N; Kishino B; Itatani H; Morii H
Department of Nuclear Medicine, Sumitomo Hospital, Osaka-shi, Japan.
Radioisotopes (JAPAN) Jul 1988, 37 (7) p402-5, ISSN 0033-8303 Journal Code: RBE
Languages: JAPANESE Summary Languages: ENGLISH
Document type: JOURNAL ARTICLE English Abstract
Two-site immunoradiometric assay for human parathyrin (PTH1-84) is specific for the intact, secreted, biologically %%%active%%% 84 amino peptide. This system incorporates two-different polyclonal %%%antibodies%%% to human intact %%%PTH%%% and has several technical advantages for use. This assay could detect a wide range of PTH in patients with hypo-, hyperparathyroidism, chronic renal failure and hypercalcemia with malignancy, especially distinguishing the level of human intact PTH in hypoparathyroidism from in normal.

6/7/24
DIALOG(R)File 155:MEDLINE(R)

05226616 89022255
Characteristics of parathyroid hormone-specific cyclic changes of glucose-6-phosphate dehydrogenase activity in the distal convoluted tubule of the guinea pig.
Sakaguchi K; Fukase M; Kobayashi I; Fujita T
Department of Medicine, Kobe University School of Medicine, Japan.
J Bone Miner Res (UNITED STATES) Jun 1986, 1 (3) p259-65, ISSN 0884-0431 Journal Code: 130
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The effect of parathyroid hormone (PTH) on the time course of glucose-6-phosphate dehydrogenase (G6PD) activity in the distal convoluted tubule of a vitamin D-depleted guinea pig was determined using quantitative cytochemistry. G6PD activity decreased to the stable basal level 5 hrs after the initiation of the kidney segment maintenance cultures. The exposure of the tissues to 1 pg/ml of bovine PTH-(1-84) induced a cyclic change of G6PD activity, whereas neither carboxyl-terminal PTH nor other hormones tested showed such activity. After a 16-min exposure to bovine PTH-(1-84), the peak height of each cycle began to decrease until it disappeared at 34 min. The second exposure to this hormone at 46 min reinduced a similar cyclic change with a similar peak, indicating full viability of the cells. When bovine PTH-(1-84) was incubated with an excess amount of anti-bovine %%%PTH%%% %%%antibody%%%, the %%%PTH%%%-induced G6PD %%%activity%%% was completely abolished. Throughout a 14-min exposure to either human PTH-(1-84), human PTH-(1-34) or bovine PTH-(1-84), similar cyclic changes were observed with the constant peak height regardless of the dose (10(-16)-10(-12) M), although the cycle length shortened progressively as the dose was increased. They were equipotent on a molar basis between the concentrations of 10(-16) and 10(-13) M at 6 min of hormone exposure. The present data demonstrate that the cytochemical bioassay of PTH in a vitamin D-depleted animal is based on a dose-dependent difference in the time course of G6PD activity.

6/7/25
DIALOG(R)File 155:MEDLINE(R)

04723373 85177479
Parathyroid hormone-like bioactivity in a patient with severe osteitis fibrosa cystica due to malignancy: renotropic actions of a tumour extract as assessed by cytochemical bioassay.
Loveridge N; Kent GN; Heath DA; Jones EL
Clin Endocrinol (Oxf) (ENGLAND) Feb 1985, 22 (2) p135-46, ISSN 0300-0664 Journal Code: DCI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A patient is described with malignancy, hypercalcaemia and radiological evidence of severe parathyroid bone disease but undetectable concentrations of circulating immunoreactive PTH. Autopsy showed the tumour to be a metastatic bronchial carcinoid with no evidence of primary parathyroid disease. Extracts of the tumour had no PTH immunoreactivity but had high concentrations of a substance with identical activity to PTH in a cytochemical bioassay. The biological %%%activity%%% of the extract was not inhibited by %%%PTH%%% %%%antibodies%%% but was inhibited by an antagonist to %%%PTH%%% bioactivity.

6/7/26
DIALOG(R)File 155:MEDLINE(R)

04600923 82097007
Effect of treatment with glutaurine on human antibody-dependent cell-mediated cytotoxicity (ADCC).
Lang I; Feuer L; Nekam K; Torok K; Kalmar L; Gergely P
Immunol Commun (UNITED STATES) 1981, 10 (6) p499-509, ISSN 0090-0877 Journal Code: GH4
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The effects of in vitro and in vivo treatment with glutaurine, a newly discovered %%%parathyroid%%% %%%hormone%%% possessing immunostimulative %%%activity%%%, on human %%%antibody%%% -dependent cell-mediated cytotoxicity (ADCC) were studied in 15 tumor patients with healthy subjects in a xenogeneic test system using chicken erythrocytes as target cells. A marked increase in "K" cell activity was observed in 8 tumor patients with originally low cytotoxic capacity, while originally normal ADCC activity of other tumor patients and healthy subjects was not significantly influenced by glutaurine treatment. The changes in cytotoxicity were not accompanied by changes in lymphocyte populations. Incubation of effector cells with glutaurine in vitro caused no change in ADCC activity in lymphocyte populations. Some similarities between the effects of glutaurine treatment of ADCC and that of dialyzable leukocyte extracts are discussed.

6/7/27
DIALOG(R)File 155:MEDLINE(R)

03061527 79194552
Production of hybridomas secreting monoclonal antibodies against the lympholine osteoclast activating factor.
Luben RA; Mohler MA; Nedwin GE
J Clin Invest (UNITED STATES) Jul 1979, 64 (1) p337-41, ISSN 0021-9738 Journal Code: HS7
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The human lympholine osteoclast activating factor (OAF) is thought to be involved in several bone-destroying diseases. The current studies were designed to produce monoclonal antibodies against OAF for use in the subsequent design of immunoassays for OAF in clinical samples. Spleen cells from mice immunized with purified human OAF were hybridized with mouse plasmacytoma cells in vitro to yield hybridomas. Several clones of these hybridomas secreted into the culture medium antibodies, which neutralized the biological activity of OAF at dilutions as high as 1:100,000 relative to the initial culture medium. These %%%antibodies%%% did not interfere with the %%%activities%%% of %%%parathyroid%%% %%%hormone%%% in the same systems. These results represent the first report of monoclonal antibodies against a human lympholine, and validate the concept that hybridoma production is a useful technique for developing antibodies against weak or scarce antigens.

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